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Perioperative management of Diabetes Mellitus: A review.

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ABSTRACT

Introduction: Diabetes Mellitus is frequently observed in surgical patients and relates to an increase in perioperative morbidity and mortality. Disease, anesthesia and surgery result in dysglycemia (hypo and/or hyperglycemia), which is one of the worse prognostic factors. The objective of this work is to review the specific needs of the diabetic surgical patient in the perioperative period, gathering the latest information regarding its optimization.

Materials and Methods: This dissertation was elaborated from scientific articles obtained through PubMed, Google Scholar and Google, published between 2008 and 2018 and written in English or Portuguese. In the end, eighty-nine articles were used.

Results: Some measures have been proposed in order to reduce perioperative complications in the diabetic. Preoperative period: an anesthetic evaluation, discontinuation of oral antidiabetics (OADs) and fast-acting insulin, prioritization of diabetics in the surgery list, cancellation of non-urgent procedures when there are metabolic abnormalities and poor glycemic control, and promotion of gastric emptying in gastrointestinal autonomic dysfunction. Intraoperative period: the use of intravenous (IV) perfusion of insulin for glycemic control in major surgeries, the use of glycoside sera in cases of prolonged fasting and/or IV insulin perfusion, hourly glycemic monitoring, a glycemic goal between 80-180 mg/dl with correction of hyperglycemias with insulin, and the use of a rapid-sequence intubation when there is risk of aspiration. Postoperative period: the early return to oral nutrition and the restitution of OADs and insulin with the onset of food intake, multimodal analgesia and antiemetic prophylaxis, the correct transition from IV perfusion to subcutaneous insulin and pre-discharge therapeutic optimization.

Discussion: Several studies have shown a correlation between dysglycemia and postoperative morbimortality and supported its prevention; however, the ideal glycemic range and the best glycemic management strategy remain indeterminate.

Conclusion: There are controversies in this subject and a great shortage of studies that establish specific measures and universal cut-offs. There is also a need for clearer and more appropriate guidelines to minimize perioperative complications. Continuous training of health professionals on issues related to technological development in this area, such as the perioperative approach of continuous insulin infusion pumps, is essential. It is also important that diabetics have the capacity to manage their own disease, in order to facilitate their optimization in the surgical context.

Keywords: Diabetes mellitus, Perioperative, Management, Anesthesia, Preoperative, Postoperative, Surgery.

RESUMO

Introdução: A Diabetes Mellitus é frequentemente observada em pacientes cirúrgicos e condiciona um aumento da morbimortalidade perioperatória. A doença, a anestesia e a cirurgia resultam na disglicemia (hipo e/ou hiperglicemia), que é um dos fatores de pior prognóstico. O objetivo deste trabalho é rever as necessidades específicas do doente cirúrgico diabético no período perioperatório, reunindo a informação mais recente quanto à sua otimização.

Materiais e Métodos: Esta dissertação foi elaborada a partir de artigos científicos obtidos através do PubMed, Google Scholar e Google, publicados entre 2008 e 2018 e escritos em inglês ou português. No final, foram usados oitenta e nove artigos.

Resultados: Têm sido propostas algumas medidas para diminuir as complicações perioperatórias no diabético. No pré-operatório: a realização de uma avaliação anestésica, a descontinuação dos antidiabéticos orais (ADOs) e da insulina de ação rápida, a priorização de diabéticos na lista de cirurgias, o cancelamento de procedimentos não urgentes aquando de anormalidades metabólicas e mau controlo glicémico, e a promoção do esvaziamento gástrico na disfunção autonómica gastrointestinal. No intra-operatório: o uso de perfusão intravenosa (IV) de insulina para o controlo glicémico em cirurgias *major*, a utilização de soros glicosados no caso de jejum prolongado e/ou de perfusão IV de insulina, a monitorização glicémica de hora a hora, um objetivo glicémico entre os 80-180 mg/dl com correção das hiperglicemias com insulina, e a utilização de uma intubação de sequência rápida quando há risco de aspiração. No pós-operatório: o retorno precoce à nutrição oral e a restituição dos ADOs e da insulina com o início da ingestão alimentar, a analgesia multimodal e a profilaxia antiemética, a correta transição de perfusão IV para insulina subcutânea e a otimização terapêutica pré-alta.

Discussão: Vários estudos têm mostrado uma correlação entre a disglicemia e a morbimortalidade pós-operatória e suportado a sua prevenção; no entanto, o intervalo glicémico ideal e a melhor estratégia de gestão glicémica permanecem indeterminados.

Conclusão: Existem controvérsias neste tema e uma grande escassez de estudos que estabeleçam medidas específicas e *cut-offs* universais. Há também necessidade de guidelines mais claras e apropriadas, que permitam minimizar as complicações perioperatórias. É essencial a contínua formação dos profissionais de saúde relativamente a questões relacionadas com o desenvolvimento tecnológico nesta área, como é o caso da abordagem perioperatória de bombas de infusão contínua de insulina. É também importante que diabéticos tenham capacidade para gerir a sua própria doença, de modo a facilitarem a sua otimização no contexto cirúrgico.

Palavras-chave: Diabetes mellitus, Perioperatório, Abordagem, Anestesia, Pré-operatório, Pós-operatório, Cirurgia.

ABBREVIATIONS

AACE - American Association of Clinical Endocrinologists
ADA - American Diabetes Association
DM – Diabetes Mellitus
ECG - Electrocardiogram
ESA - European Society of Anaesthesiology
GFR - Glomerular filtration rate
GIK - Glucose-Insulin-Potassium
ICU - Intensive care unit
IV - Intravenous
OADs - Oral antidiabetics
POC - Point-of-care
SAMBA - Society for Ambulatory Anesthesia

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INTRODUCTION

Diabetes Mellitus (DM) is a chronic disease of high prevalence and increasing incidence, and has been identified as a major cause of global mortality [1, 2]. In 2015, the estimated prevalence of DM was 8.5% in the world population, and 13.3% in the portuguese population [3, 4]. This multifactorial epidemic is due to the increasing age of the population and the increase of obesity and sedentarism [2, 5].

DM is the most common multisystemic endocrine-metabolic disease, characterized by a dysregulation in carbohydrate metabolism where hyperglycemia predominates, and, if untreated, can become debilitating due to chronic failure of several organs [6]. It is classified based on its pathophysiological mechanism in four clinical types [6, 7]. Type 1 and type 2 DM are the most frequent types; however, type 2 is the most common (90-95% of cases) and most often develops in elderly and/or obese adults [1, 2]. Type 1 mainly affected pediatric patients [8].

In DM there are several progressive physiological changes, thus, some systems must be emphasized in the anesthetic approach: musculoskeletal, renal, neurologic, and cardiovascular [9].

Musculoskeletal system

Chronic hyperglycemia leads to abnormal cross-linking of joint glycogen, which will limit joint mobility, triggering Stiff Joint Syndrome or diabetic cheiroarthropathy, which mainly affects the temporomandibular, atlanto-occipital and cervical spine joints. Diabetic scleredema is characterized by a non-depressible hardening of the skin in the neck and upper back regions and, associated with reduced joint mobility, limits the angles of movement of the neck and may hinder orotracheal intubation [9].

Renal system

A significant proportion of patients with DM have diabetic nephropathy, which is characterized by the development of albuminuria and progressive reduction of renal function [9].

Neurologic system

Approximately 10% of diabetics have symptoms of peripheral diabetic neuropathy, that is mainly caused by hyperglycemia, which leads to neuronal damage and decreased conduction velocity and nerve fiber reactivity [10].

Autonomic diabetic neuropathy is a common complication of DM and is frequently undiagnosed, affecting the gastrointestinal, genitourinary and cardiovascular systems [9]. It is

characterized by resting tachycardia, exercise intolerance, orthostatic hypotension, asymptomatic involvement of the coronary arteries, arrhythmias and sudden cardiac death. Autonomic gastrointestinal neuropathy causes symptoms such as dysphagia and gastroparesis. Autonomic genitourinary neuropathy main clinical manifestations are neurogenic bladder and sexual dysfunction [11]. Impaired neurovascular function, loss of autonomic response to hypoglycaemia and affected thermoregulatory response to hypothermia during anesthesia are also possible [5, 9].

Cardiovascular system

Diabetics are at increased risk of hypertension, coronary artery disease, peripheral arterial disease, silent myocardial ischemia, QT interval abnormalities, arrhythmias, cardiomyopathy, heart failure, and sudden death. Through several mechanisms, hyperglycemia promotes vasodilation and induces a pro-inflammatory, prothrombotic and pro-atherogenic state, responsible for these complications. These patients also have high intraoperative cardiovascular instability, since neuropathy predisposes them to bradycardia and hypotension during general anesthesia. The cardiovascular disease is being the cause of death in 80% of diabetics [5, 9, 12].

The estimated incidence of diabetics requiring surgery is about 25%, which explains why DM is frequently observed in surgical patients [11]. As the incidence of this disease continues to increase, and diabetics more often suffer from macro and microvascular complications and other comorbidities, their increased need for surgical procedures is understandable [13]. DM leads to increased morbidity, perioperative mortality (50% higher than non-diabetic patients) and use of resources, leading to more frequent and prolonged hospitalizations [9, 14]. The determinants of worse prognosis of diabetics in the perioperative period are many, namely: comorbidities; the acute complications of diabetes; the complex medication regimens; errors in insulin prescription; the perioperative infections; failure in identifying diabetics; the lack of adequate institutional therapeutic protocols; and the lack of knowledge about the correct approach [9, 15]. Acute disease, anesthesia and surgery result in metabolic disturbances and in dysglycemia, one of the factors with the worst prognosis [16, 17].

Hyperglycemia

Hyperglycemia is defined as glycemia > 140 mg/dl in the hospitalized patient [18]. During surgery and postoperative period, depending on the type of anesthesia and surgery, nutritional and fluid support and anatomical location, glycemia increases and may be responsible for perioperative complications [19]. As the ability to respond to the need for insulin is reduced or

absent in diabetics, the risk of developing hyperglycemia is greater [20]. However, even in people without DM, surgical stress can lead to transient hyperglycemia that normalizes after stabilization of the acute event, but which in some cases may lead to later disease development [19, 21]. Stress is the main etiology of perioperative hyperglycemia, followed by iatrogenic causes such as discontinuation of medication, drugs, immobilization and advanced age of the patient. Thus, hyperglycemia results mainly from insulin resistance and relative hypoinsulinemia, triggered by the release of pro-inflammatory mediators and counter-regulating hormones, which is triggered by stress, tissue trauma, fasting and pain [1, 2, 22]. This combination constitutes a serious problem of maintenance of glucose homeostasis, particularly in diabetics with poor metabolic control [2, 13]. Thus, in extreme cases, acute complications of DM can be precipitated due to metabolic decompensation, resulting in diabetic ketoacidosis or hyperosmolar hyperglycaemic syndrome [9]. In addition, persistent hyperglycemia, as well as sustained hyperglycemia (estimated by HbA1c), are also risk factors for the occurrence of sepsis, acute renal injury, alteration in operative wound healing, ischemia, infections, and mortality [1, 2, 22, 23]. Thus, hyperglycemia accounts for 66% of postoperative complications and 25% of perioperative deaths [2, 24].

Hypoglycemia

Hypoglycemia (< 70 mg/dl) is common in hospitalized diabetics, occurring more frequently in type 1 DM [17, 22, 25]. Since glucose is the metabolic substrate required for the brain, this hypoglycemic state leads to neuroglycopenia and may result in irreversible neurological damage and coma, and is also associated with an increase in mortality, length of hospital stay, risk of infection, difficulty in healing, prolongation of the QT interval, ischemia, arrhythmias and sudden death [16, 26]. During general anesthesia or sedation, the symptoms of hypoglycemia are masked and, therefore, the prevention of their occurrence is of high importance [23].

The objective of this work is to review the specific needs of DM in the perioperative period and its effective approach, gathering the latest information regarding the optimization of the diabetic surgical patient.

MATERIALS AND METHODS

This dissertation was elaborated from scientific articles obtained through the bibliographic research carried out on the PubMed, Google Scholar and Google platforms between October 2018 and December 2018. The combinations of terms used in this research were: Diabetes anesthesia surgery, Diabetes postoperative anesthesia, Diabetes preoperative anesthesia, Diabetes perioperative management, Diabetes anesthesia management, Diabetes anesthesia.

The types of articles used in this work were reviews, systematic reviews, case reports, guidelines and observational studies. Articles published between 2008 and 2018 and written in english or portuguese were included. Moreover, only studies conducted in humans were used. This research resulted in a thousand and one articles.

The articles were initially selected by the reading of the abstract and later by its complete reading. At this stage, were excluded studies based only in child or elderly population; studies related to specific features and specificities of treatment of abnormalities existing in DM; studies related to specific features of DM but not focusing on this pathology; studies about special needs but not related to DM; studies about hospital management; articles about etiological issues and DM pathophysiology; articles referring to individuals with other specific pathologies; as well as those that addressed other types of DM besides type 1 and 2 DM (such as gestational DM or DM due to genetic defects of β cells, diseases of the exocrine pancreas, endocrinopathies and drugs); and that were focused on specific surgery procedures or about specific surgical details.

With the application of these inclusion and exclusion criteria, one hundred and sixty-six publications were obtained.

Lastly, other articles were also analyzed, by consulting the bibliographic references of those initially selected, which also took into account the year of publication. In the end, we used eighty-nine scientific articles in this bibliographic review.

RESULTS

Given the increased risk of complications and the need for specific care, a correct perioperative approach of the diabetic is crucial [11]. This approach may take on some differences, depending on the type of DM, the evolutionary state of the disease and whether there are target organ lesions, and comprises 3 phases: preoperative, intraoperative and postoperative [1, 2].

Preoperative

There are some things to be considered during this period, concerning diet, medication, level of diabetes control and pre-existing complications [27]. In elective surgery, the objectives are to ensure that DM is as well controlled as possible and to avoid delays in surgery, minimizing the fasting period, ensuring normoglycemia and altering as little as possible the normal routine of the patient [15].

Anesthesia consultation

The guidelines recommend that diabetics, when proposed for elective surgery, should be evaluated prior to anesthesia [28, 29]. If they have been referenced by primary care, if possible, the patients should also be optimized by them [15], since according to the Society for Ambulatory Anesthesia (SAMBA) [23], the desirable glycemic control should ideally be achieved in the weeks prior to surgery.

Thus, this consultation should begin with a detailed clinical history of the type of DM and the dose of antidiabetic therapy, the duration, complications and comorbidities known, evaluation of prior metabolic control (through glycemic self-monitoring, mean blood glucose values and HbA1c) and the presence of recent hypoglycemias [22, 23].

Therefore, if HbA1c dosing has not been done or patients report poor glycemic control, HbA1c's assessment will reflect the mean glycemia in the last 3 to 4 months, being a good indicator of long-term glycemic control [8, 30, 31]. An HbA1c < 7% gives us the assurance that the patient has a well-controlled diabetes [29].

Moitra et al. [32] also concluded that Hb1Ac levels predict pre and postoperative blood glucose levels, and Gustafsson et al. [33] have shown that the preoperative measurement of HbA1c may identify patients at high risk of postoperative hyperglycemia and complications. Therefore, when it is elevated, it may be necessary to postpone elective surgery for medical optimization, with the guidelines advising this postponement with HbA1c ≥ 8.5-9% [1, 22]. On the

other hand, HbA1c < 5% probably indicates severe recurrent hypoglycemias, being it usually advisable to postpone surgery [13]. However, there may be situations in which it is not possible to promote glycemic control preoperatively, being it possibly acceptable to proceed with surgery after explaining all risks to the patient and evaluating the urgency of the procedure [15, 34].

When unidentified as diabetic, surgical patients should be screened for all possible risk factors for undiagnosed DM, such as obesity, metabolic syndrome, diabetogenic drugs, personal history of gestational DM or transient hyperglycemia, family history and suggestive symptoms. When there is a suspicion, HbA1c dosing should be considered [8, 13]. If this test is not performed before, it may be performed during hospitalization after hyperglycemia is observed [16].

In the consultation, instructions should also be given on the management of antidiabetic medication, the control of perioperative dysglycemia and the likely effects of surgery on glycemic control [15]. Patients should be informed that smoking cessation is recommended and that, on the eve of surgery, they should maintain their usual diet [8, 29]. According to the European Society of Anaesthesiology (ESA) [35], it is recommended that diabetics be without solid food intake within 6 hours prior to elective surgery (if the risk of aspiration is very high, the fasting period may be prolonged) [8]. They should also be advised to take their usual medication and therapy for hypoglycaemic seizures [22, 23].

It is also important to assess the patient's ability to manage their own diabetes, because if he is able to monitor glycemic levels and follow medication adjustment instructions, the perioperative glycemic targets are more easily reached [23, 31].

The American College of Cardiology and the American Heart Association [36] also recommend the execution of an electrocardiogram (ECG) in all diabetics, except for procedures with low surgical risk. The fasting lipid profile, hepatic and renal function, and electrolytes are also mandatory preoperative tests [29].

Management of antidiabetic treatment

With proper guidance, diabetics should be allowed to maintain control and continue self-administration of their medication [15].

Oral antidiabetics (OADs) have a slow onset and long duration of action and may lead to unexpected clinical variations in hospitalized patients [29].

Metformin is a renal excreted biguanide, that can cause hemodynamic instability and decrease in intraoperative renal perfusion, which also predisposes to lactic acidosis, being it classically recommended that it be discontinued within 24 to 48 hours prior to surgery or elective radiological procedure [8, 37]. The American Association of Clinical Endocrinologists (AACE) and

the American Diabetes Association (ADA) [31] do not recommend its use in hospitalized patients because of the risk of renal damage, hemodynamic instability and possible need for contrast administration in procedures. However, some recent guidelines state that metformin can be safe and continued until the night before surgery if there is no altered renal function (glomerular filtration rate (GFR) < 30 ml/min) or a significant risk of acute kidney injury (dehydration, procedures with risk of hypoperfusion and hypoxia, and use of contrast) [1, 15, 16, 22].

Due to the possibility of ketoacidosis in fasting diabetics on SGLT-2 inhibitors, these drugs are suspended [22].

Insulin secretagogues, such as sulfonylureas and meglitinides, are usually withdrawn in the morning of surgery, due to the risk of hypoglycemia in fasting patients or with impaired renal function [8, 15, 16].

Alpha-glucosidase inhibitors decrease glucose absorption after meals, having no effect on preoperative fasting states, with its discontinuation being recommended [37].

Thiazolidinediones are also discontinued on the day of surgery, as they may cause fluid retention in the postoperative period [37, 38].

Injectable GLP-1 agonist OADs can be maintained on the day of surgery if necessary, as well as DPP-4 inhibitors, as there is no risk of hypoglycemia even in fasted patients, however, this type of drug reduces postprandial blood glucose and its effects will be reduced, also causing gastroparesis, and are therefore often withdrawn on the day of surgery [16, 38].

Basal insulin is generally used to maintain stable glycemic levels and is not associated with hypoglycemia even during fasting [23]. Demma et al. [39], in a recent study with diabetics treated with glargine insulin once a day, concluded that the group that administered 60-87% of the normal dose in the afternoon before surgery had the highest percentage of cases (78%) within the target range of glycemia values (100-180 mg/dl) ($P < 0.001$) and a lower number of cases of hypoglycemia, compared to the group that did not administer insulin or that administered the normal dose. Thus, in order to avoid hyperglycemia and ketoacidosis, many guidelines, such as AACE/ADA [31], Endocrine Society [40], SAMBA [23] and Joint British Diabetes Societies [34] recommend the continuation of long-acting insulin in the usual dosage (or 80% of the dose, if at risk of morning hypoglycaemia) in the night before, or 75-100% of the dose (depending on the risk) if administered in the morning of the surgery [41].

For other types of insulin, guidelines recommend that patients, in the morning of the surgery, take 50-75% of the intermediate insulin (NPH) dose, or the total dose if administered the night before (or 75-80% of the dose, if risk of morning hypoglycaemia), and advise against the administration of fast-acting insulin in the morning of surgery [13, 23, 34, 41].

SAMBA [23] warns that preoperative insulin management plans should take into account

the level of glycemic control because, for example, patients with strict control, more unstable values or the use of complex insulin regimens, are at higher risk of hypoglycemia during fasting.

These adjustments should also take into account the fasting and surgery time and the expected time to start normal feeding after surgery [23].

In emergency surgeries, by definition, there is no opportunity for a plan to be performed [15]. In ambulatory surgery, OADs can be continued if the patient is controlled [13].

Surgical admission plan

Diabetics should preferably be scheduled for the start of the surgical shift or as early as possible in order to minimize the fasting period and the risk of hypoglycaemia [15, 28].

According to the Joint British Diabetes Societies [34], when possible, admission should be planned for the day of surgery. Diabetics undergoing major surgery should be hospitalized the day before or when they start fasting, in order to initiate insulin infusion [29].

In diabetics, ambulatory surgery should be considered as it allows to reduce the risk of iatrogenic complications, however, these should be well controlled and able to manage their own diabetes, and surgery should be achievable in this context [1, 29]. According to SAMBA [23], the decision to go through with ambulatory surgery in patients with poor glycemic control should take into account the comorbidities and potential risks of surgery. These surgeries follow the protocols of minor surgeries [29].

Urgent surgeries follow the protocols of major surgeries [26].

Preoperative evaluation

Preoperative urine collection II is recommended for the detection of asymptomatic urinary infections and proteinuria associated with acute postoperative renal failure in patients with risk factors (advanced age, type 1 DM and pre-existing renal disease) [29]. Adequate preoperative hydration (with water up to 2 hours prior to surgery) and initiation of fluid replacement (≥ 2 hours before induction) helps prevent postoperative dehydration [13, 23].

If there are symptoms of dehydration, diabetic ketoacidosis or hyperosmolar hyperglycemic state, gasimetry and electrolytes should always be requested [8].

Diabetics undergoing emergency surgery are rarely well metabolically controlled, and the evaluation should include pH, creatinine and urea, and the volumetric status, in addition to electrolytes, with potassium and acidosis alterations being the priority corrections [29].

Blood glucose monitoring

Especially in patients undergoing long procedures and with a high metabolic impact,

blood glucose levels should be monitored at admission [8, 16]. Frequent monitoring of blood glucose should be performed every 2 to 4 hours in all fasting patients [26, 38].

Hypoglycemia

Preventive measures of hypoglycemia include the identification of patients at increased risk (under intensive therapy, with oscillating glycemic profile, history of frequent hypoglycemia, and elderly patients), their monitoring and the appropriate preoperative changes in antidiabetic therapy [23, 42].

Patients should be advised to carry a form of glucose that can be administered in the event of hypoglycemia during fasting and that does not lead to the cancelling of surgery, such as sugar-rich drinks [15, 23]. ESA [35] defines safe administration of these beverages as up to 2 hours prior to elective surgery. However, researchers are always reluctant to give these formulations due to possible effects on blood glucose and gastric emptying. Gustafsson et al. [43] concluded that the intake of a carbohydrate-rich drink is safe in diabetics, without risk of hyperglycemia and aspiration, when performed in the 180 minutes prior to anesthesia.

Glucose pills may also be used in case of hypoglycemia, although some anesthesiologists do not recommend its use within 6 hours prior to surgery [15, 23]. Thus, if the patient presents with hypoglycemia in the last minutes before surgery, this should be corrected with 3-9 g of intravenous (IV) glucose, and surgery should proceed with regular monitoring of glycemia [16, 29]. In case of severe hypoglycemia, elective surgery may have to be postponed [13].

Hyperglycemia

Discontinuation of antidiabetic medication, inadequate long-term glycemic control, and preoperative response to stress may be the cause of preoperative hyperglycemia. This should be corrected before surgery with fast-acting insulin (safer due to shorter duration of action) in sliding-scale (corrective insulin scheme based on a stratified adjustment scale), usually by subcutaneous administration, but it can be administered intravenously in case of more invasive procedures, and, if controllable, surgery should not be cancelled [8, 23, 29, 38].

There is no consensus as to when surgery should not be performed due to hyperglycemia, but according to SAMBA and other recommendations, surgeries, except for life-threatening, should be postponed for at least 12 hours in patients with compromised metabolic status (diabetic ketoacidosis, hyperosmolar hyperglycemic syndrome or severe dehydration), and metabolic abnormality and glycemia should be corrected before surgery [16, 23]. Thus, if glycemia > 250-300 mg/dl, the presence of ketonemia and/or ketonuria should be evaluated [15]. In case of glycemia < 250-300 mg/dl and in the absence of metabolic changes, sliding-scale insulin infusion

should be used and if levels drop as expected within one hour, surgery can proceed normally [16]. Recommendations usually advise the postponement of non-urgent surgeries in case of persistent hyperglycemia above 300-500 mg/dl, there being no sufficient evidence to suggest a specific cut-off [16, 37, 44].

Diabetics' identification is imperative, however, about one-third remain undiagnosed and untreated prior to surgery [13, 37]. In the presence of hyperglycemia without previous diagnosis of DM, this may be due to hyperglycemia of stress, and the determination of HbA1c may allow to make this distinction [31].

Management of the continuous subcutaneous insulin infusion system

The use of insulin infusion pumps has increased in recent years and hence the importance of a better knowledge about its perioperative approach [8].

The use of an infusion pump has been demonstrated to be successful in hospital context [45, 46]. Corney et al. [47], carried out an investigation with ambulatory controlled diabetics with continuous insulin infusion pumps, which were grouped according to the intraoperative insulin infusion method and which revealed that the group that suspended the infusion pump experienced a higher percentage of intraoperative blood glucose ≥ 179 mg/dl (84.2%). There was no significant difference in mean intraoperative blood glucose between the infusion pump group and the IV infusion group (P=0.128).

Thus, the authors indicate that in minor elective procedures, especially shorter (< 2h) and/or with short fasting period, the patient can maintain this administration route. In urgent surgeries or with a long fasting period, the IV infusion regimen will be immediately established [8, 22].

In preparing for surgery, it is recommended to optimize the basal insulin dose in order to maintain stable fasting blood glucose values and to place the catheter far from the surgical field. On the day of surgery, this baseline rate should be maintained, and if there was no appropriate dose adjustment, the flow rate could be reduced by 20% [22, 23].

A specialist in this area should be involved in these decisions [40, 48].

Musculoskeletal system

Standard airway assessment techniques are appropriate in DM but do not identify all difficulties in intubation, and it is advisable to use the prayer sign (both hands together and with the palms facing, being positive when there is an inability to approach them) to identify the existence of diabetic cheiroarthropathy and the difficulty of intubation, placement of venous

access and positioning of the patient [8, 13]. Kundra et al. [49], to evaluate the perioperative morbidity associated with the positivity of this test, carried out a recent study that showed that in the group with positive prayer sign the average hours of ventilation was superior (P=0.013) and that the mean length of hospital stay was also higher (P <0.0001).

Renal system

Preoperative assessment of the albumin-creatinine ratio and GFR is essential in major surgery, emergencies or patients with poor glycemic control. In the presence of chronic diabetic renal disease, it is necessary to avoid the administration of nephrotoxic agents and hemodynamically optimize the patient for blood pressure averaging between 60-70 mmHg in order to maintain renal perfusion [50].

Neurological system

The evaluation of the existence of autonomic cardiac dysfunction involves simple tests using the Valsalva maneuver and evaluation of changes in heart rate and blood pressure when moving from supine position to sitting or in response to deep breathing. If neuropathy is diagnosed, drugs that induce orthostatic hypotension should be avoided and the QT interval should be evaluated with a simple ECG [51, 52].

Gastroparesis, with delay in emptying and gastric dilation, is characteristic of the autonomic gastrointestinal neuropathy and a risk factor for aspiration and consequent chemical pneumonitis. During the anesthetic consultation, the patient should be questioned about classic clinical manifestations, and if clinically suggestive, gastric antrum and residue should be measured by ultrasound. Some recommendations to reduce the risk of regurgitation and aspiration during induction of anesthesia include avoiding solid food intake and promoting gastric emptying in the preoperative period with a prokinetic (metoclopramide or erythromycin) [8, 13].

In diabetic patients submitted to local-regional techniques, it is prudent to evaluate the extent of autonomic, motor and sensory neuropathy [29].

Cardiovascular system

A preoperative cardiovascular assessment should be performed with blood pressure and heart rate measurements, search for signs and symptoms of heart failure, cerebrovascular and peripheral vascular disease, as well as the presence of diabetic foot and peripheral neuropathy [8]. Joint British Diabetes Societies [34] recommend pressure relief in case of high-risk feet and avoidance of anti-embolism stockings in case of vascular disease or peripheral neuropathy. According to the European Society of Cardiology and the European Association for the Study of

Diabetes [53], the evaluation of heart disease with more invasive examinations should be performed only in patients at high cardiovascular risk. Patient positioning should also be slow and controlled to avoid a sudden drop in blood pressure [11].

Intraoperative

The objective of intraoperative care is to maintain a good glycemic control and a normal concentration of electrolytes, while also optimizing cardiovascular function and renal perfusion [15].

Glycemic control

Clinicians should take into account the time taken to complete the procedure when determining the intraoperative glycemic control strategy [38].

Given the action profile and the multiple contraindications to the in-hospital use of OADs, insulin therapy with continuous infusion or bolus is the correct option for the perioperative control of glycemia [29].

As subcutaneous insulin may be associated with a decrease in its absorption in case of hypothermia or peripheral vasoconstriction, when undergoing major surgery, patient's glycemia should be controlled through IV infusion of regular insulin, which should be started preoperatively if possible [1, 29, 38]. This regular insulin remains physiologically active for approximately one hour but has a half-life of 7 minutes, which allows for an adequate glycemic control, countering unexpected changes in blood glucose [38].

Typically, in DM type 1, lower insulin doses are required compared to insulin-treated type 2 DM, in order to obtain adequate glycemic control [2]. Thus, in type 1 diabetics, the rate of insulin infusion starts at about 0.5-1 U/hour, while the infusion rate typically increases in type 2 DM or poorly controlled diabetics, from 1-2 U/h up to about 2-3 U/h or more [22, 37]. Sliding-scale subcutaneous insulin, used for hyperglycemia, should not be used as monotherapy because of the high risk of hypoglycemia and inferior glycemic control [1, 54].

According to the Joint British Diabetes Societies [34], if the fasting period is short, and the patient is controlled and able to manage diabetes after surgery, a correct manipulation of the antidiabetic medication may be sufficient to allow glycemic control in elective surgery. Thus, in minor surgery, if preoperatively controlled (fasting glycemia < 180 mg/dl), they take intraoperative rapid correction insulin only if necessary, IV in bolus or subcutaneous. If uncontrolled, they should also initiate IV infusion of insulin [1, 22, 29].

Fluid and electrolyte management

Adequate intraoperative administration of crystalloids helps prevent dehydration [23].

During surgery, the replacement fluids should not contain glucose unless there is low blood glucose, as the tendency is for hyperglycemia. However, it is important to avoid hyperchloremic metabolic acidosis, being it advisable do administrate, at 100-125 ml/hr, Hartmann's solution or other isotonic crystalloid solution (0.9% NaCl, for example) [15, 22]. Hartmann's solutions are recognized as safe in diabetics [55].

However, if prolonged fasting is predicted and if patients are taking IV insulin infusions, 5-10% glycated sera should be given at 100-125 ml/h to avoid catabolism, hunger ketosis and hypoglycemia [29].

Administration of electrolytes may also be necessary, especially to avoid insulin-induced hypokalemia, and potassium should be evaluated every 4 hours (or every 1 hour if there are changes in insulin flow), and if necessary, KCL may be administered with electrocardiographic monitoring [13, 26].

In addition, there is a continuous Glucose-Insulin-Potassium (GIK) infusion technique, which has been supported as inotropic and metabolic therapy in severe critical disease states [56]. However, this method is not authorized for individual manipulation of glucose or insulin levels and is best suited for maintenance of glycemia after reaching a specific target, with the use of IV insulin infusion having more advantages [34, 37].

Target glycemic range

The management of perioperative glucose levels revolves around a few goals: to reduce morbidity and mortality, to avoid severe dysglycemia, to maintain fluid and electrolyte balance, and to establish safe glycemic targets [38].

However, there is controversy regarding the target glycemic range to be achieved during this period. Early studies in this area suggested that intensive glycemic control (80-110 mg/dl) had a positive prognostic impact, but there is currently evidence that it should not be widely recommended [22, 57]. According to the ADA's most current recommendations [58], the glycemic target should be between 80-180 mg/dl and more specifically < 180 mg/dl in the critical patient and < 140 mg/dl in the stable patient [31]. In patients with a history of poor metabolic control, SAMBA [23] recommends maintenance of preoperative baseline values instead of attempting to normalize blood glucose levels.

Blood glucose monitoring

Adequate blood glucose monitoring is critical in maintaining patient safety, facilitates

insulin titration, and allows the early detection of hypoglycemia [23].

Blood glucose measurements should ideally be performed using arterial and venous blood instead of capillary blood and point-of-care devices (POC), as these may show results altered by poor peripheral perfusion, hypovolemia, shock, hypothermia and/or acid-base disorders [8, 13]. Several studies recommend against the use of POC in the perioperative and the preferential use of glycemic measurements through central-laboratory devices, since the latter have better accuracy [59, 60]. Thus, the use of POC may not be appropriate in patients undergoing major surgery [8], however, in stable patients, they correlate well with laboratory values [61] and therefore, in general, during surgery, glycemic levels are monitored through POC [37].

The guidelines recommend that blood glucose be monitored intraoperatively every hour (or every 2 hours in stable patients) during major surgery or minor surgery in poorly controlled insulin takers, and at least once in minor surgery [13, 29]. It should be monitored more frequently in emergency surgeries or if the values are outside the target range or suffer a sharp variation (hypoglycemia or changes in the rate of insulin infusion) [13, 37]. It should also be evaluated before induction of anesthesia [15].

Hypoglycemia

Hypoglycemia is more likely in the intraoperative period due to fasting, and during anesthesia it may not be recognized, which explains the need for frequent monitoring and its early detection [16].

If glycemia ≤ 70 mg/dl, the IV infusion of insulin should be discontinued and reevaluated within 5-10 minutes and if it persists initiate 3-9 g of IV hypertonic glucose and evaluate glycemia 15-20 minutes later. The guidelines state that insulin infusion can be resumed at a lower rate when glycemia > 100 mg/dl in two consecutive measurements [16, 22, 29].

Hyperglycemia

In case of intraoperative hyperglycemia in minor surgical procedures, it should be corrected with sliding-scale insulin, preferably subcutaneously (for ease and efficacy), and in major surgeries by increasing the IV infusion rate. If two doses of subcutaneous insulin do not allow reaching the target glycemic range, IV infusion should also be initiated [15, 16, 23, 40].

In diabetics, fast-acting subcutaneous insulin should be given up to a maximum of 6 U [15, 16]. This administration is done according to sliding-scale protocols, assuming that 1 U should lower about 50 mg/dl of glucose, or according to the patient's insulin sensitivity factor, being careful not to administer the new dose until the peak of action of the previous dose has passed (2-4 h) [1, 22].

Management of the continuous subcutaneous insulin infusion system

In the operative room, the anesthesia team assumes responsibility for the infusion pump [1, 22].

Blood glucose should be checked every hour and, if necessary, corrective insulin should be given. However, if uncontrolled hyperglycemia, it may be necessary to convert to IV insulin infusion [1, 22].

In case of hypoglycemia, an infusion of glucose should be administered, and if this persists, the switch should be made to infusion of IV insulin with glycated serum [1].

Type of anesthesia

It is crucial that the anesthetic technique used allows a rapid post-surgical recovery and the selection should be made based on the coexistence of other diseases [37].

The type of anesthesia influences the hyperglycemic response. While the most commonly used anesthetic agents cause hyperglycemia, epidural or local anesthesia tends to have a nominal effect on glucose metabolism by inhibiting the release of catecholamines, attenuating the response to surgical stress [37]. Li et al. [62] showed that, compared to general anesthesia, the combination of general and epidural anesthesia was associated with better intraoperative glycemic control.

In general, the response to neuromuscular blocking agents is normal in diabetics, but in patients with irregular neuromuscular transmission, hemodynamic instability due to severe hypotension and possible increase of the risk of neuropathy after peripheral nerve block may occur [11, 37]. However, loco-regional techniques are not contraindicated in diabetics and have some advantages, such as avoiding orotracheal intubation, allowing the evaluation of the central effects of hypoglycemia and the recovery of oral intake earlier [29].

Renal system

In the presence of chronic diabetic renal disease, hemodynamic monitoring is recommended to evaluate the volume and guide the need for vascular filling and administration of vasopressors in case of risk of instability. The administration of anesthetic agents should also take into account the pharmacokinetic and pharmacodynamic changes resulting from this complication [13].

Neurological system

The hemodynamic response to intubation is altered in diabetics with autonomic neuropathy, and therefore, must be executed with careful monitoring, titrated anesthesia and

minimal manipulation of the airway [11]. In patients with a high risk of gastroparesis and aspiration, it is important to consider the use of a rapid-sequence intubation [63].

Cardiovascular system

In diabetics with autonomic cardiac neuropathy, hemodynamic status influences the titration of anesthesia, requiring continuous monitoring of blood pressure and heart rate, ECG to identify rhythm disturbances and ischemic changes, and central venous pressure to assess volume. In these patients with cardiovascular instability, but subject to neuraxial central anesthesia, ultrasound-guided nerve block is safer [11].

Postoperative

Resumption of food intake

Diabetics undergoing major surgery resume oral ingestion more than 4 hours after surgery, and those undergoing minor surgery less than 4 hours [29].

If the patient is unable to tolerate oral nutrition for a long period of time, total parenteral nutrition should be considered, and enteral nutrition should be resumed as soon as possible [64]. However, in patients treated with intra-operative IV insulin, it will be more advisable to continue the infusion of insulin together with an infusion of glucose until they are able to tolerate oral feeding [37].

Control of pain, nausea and vomiting

According to the Association of Anaesthetists of Great Britain and Ireland [15], postoperative multimodal analgesia should be used along with appropriate antiemetic prophylaxis to allow an early return to normal diet and antidiabetic regimen, promoting a more precocious hospital discharge.

One of the most important and validated antiemetics for perioperative use is dexamethasone, which increases the risk of hyperglycemia, being it recommended to use in combination with another antiemetic (droperidol or 5-HT3 antagonist) [8, 13, 23]. Glycemic measurement should be ensured every hour up to 4 hours after dexamethasone administration [15].

Poorly controlled pain is also a risk factor for hyperglycemia, with common analgesics not affecting glycemic control and able to be used without modifying the indication or dose. The use of local anesthesia is also associated with better postoperative pain control [13, 29].

Blood glucose monitoring

Shortly after surgery, capillary glycemia should always be evaluated [16, 22]. In major surgeries, blood glucose should continue to be monitored hourly until 4 hours postoperatively [16, 29]. In subjects undergoing minor surgery, it should be monitored at the end of the fast or 4 hours after surgery [29].

Target glycemic range

According to the guidelines, the postoperative target glycemic range is 140-180 mg/dl [37]. However, if patients are monitored in an intensive care unit (ICU) after surgery due to complications or comorbidities, the hyperglycemic response to stress (mean blood glucose of 180-220 mg/dl) should be taken into account and a strategy with more tolerant glycemic management should be developed [65].

Hypoglycemia

The risk of hypoglycemia remains up to 1,5-3 hours after the last insulin dose, and its occurrence should be monitored [13, 42].

When capillary glycemia ≤ 70 mg/dl and there is no contraindication for oral feeding, the patient should ingest about 15 g of sugar and measure glucose 15 minutes later, repeat if levels remain low and, if necessary, IV hypertonic glucose may be administered [16, 22]. If oral feeding is not indicated or the patient is unconscious, IV infusion of glucose or administration of subcutaneous glucagon (if there is no IV access) should be done immediately [23, 37].

Hyperglycemia

Due to the stress, postoperative complications and the side effects of anesthesia, there is usually an elevation of glycemia and difficult glycemic control in this period [8, 37].

If blood glucose > 180 mg/dl, corrective insulin should be administered [16]. If glycemia > 250-300 mg/dl in patients treated with insulin, the presence of ketosis should be investigated and, if present, hydration and rapid insulin analogue should be rapidly initiated. If present in type 2 diabetics, electrolytes should be dosed to confirm the presence of hyperosmolar syndrome and refer to the ICU [13].

Management of antidiabetic treatment

When the patient is able to safely resume food intake without nausea or vomiting, the infusion of IV insulin may be terminated and the glycemic control procedures applied before surgery may be restored, being it possible that they have to be adjusted [37].

The basal-bolus scheme is the most adequate and safe for the postoperative period [13, 66]. The literature recommends that the transition from IV to subcutaneous insulin occurs early (after the patient has stable glycemia and without vasopressors) and with overlapping of the two types of insulin, to assure a basal insulin concentration, preventing ketoacidosis, and to increase glycemic control [37, 38]. An insulin-dependent diabetic should continue IV infusion of insulin at least 30 to 60 minutes after the first dose of fast-acting subcutaneous insulin (administered with a meal) [1, 15], and at least 2 to 4 hours after the administration of long-acting insulin (if it had been stopped) [16]. In this transition, the subcutaneous basal insulin dose corresponds to approximately 50-80% of the total dose of IV insulin administered within 24 hours of intraoperative [29, 38, 67]. Postprandial insulin requirements for rapid insulin bolus should be assessed according to how the patient is being nourished [37]. The recommendations of ADA/AACE [31] are that, of the total subcutaneous dose, 70% is given as baseline and 30% as a prandial dose in the postoperative.

In non-insulin-dependent type 2 diabetics or non-diabetics, whose blood glucose levels were controlled with low insulin infusions (≤ 2 U/h), no transition is needed, with just adequate glycemic monitoring and subcutaneous insulin correction boluses being maintained if necessary [16, 29].

If IV infusion of insulin was given in a short period of time, to a patient not previously treated with insulin, but postoperative glycemic levels remain high, it is correct to initiate insulin at the daily dose of 0.5-1 U/kg [13].

Concerning OADs, the guidelines advise the commencement of preoperative doses at the beginning of food intake, and it may be necessary to reduce or delay the intake of sulfonylureas if food intake is likely to be reduced [15, 23]. The exception is metformin, which, when there is suspicion of renal hypoperfusion or 24 hours after major surgery, is resumed only after verification of a GFR > 60 ml/min [29, 68]. Documentation of adequate renal function is also required in the resumption of SGLT-2 inhibitors [22].

In the case of diabetics without previous diagnosis, the possibility of initiation of OAD and dietary recommendations is advised, and a consultation should be scheduled [13].

Decisions regarding the ambulatory DM treatment regimen should be based on renal function, dietary intake, general functional status and type of surgical procedure performed [8], and the patient should be involved in this planning [15].

Management of the continuous subcutaneous insulin infusion system

If the patient maintained the system intraoperatively, in the postoperative period he should start prandial bolus according to the usual scheme, once he starts oral ingestion [22].

If it has not been maintained, the pump must be reconnected if the patient is able to handle it independently. If the patient is not autonomous, it is mandatory to start a bolus-basal scheme with subcutaneous insulin [13].

Pre-discharge evaluation

Before discharge, the capillary glycemia should be checked [22, 23]. If glycemia ≤ 180 mg/dl, patient can be discharged; if glycemia > 180 mg/dl, rapid insulin bolus should be given and discharge should be postponed until stabilization; and if glycemia > 300 mg/dl, discharge is contraindicated and the patient is admitted for IV infusion of insulin [13]. Discharge should not be delayed only because of poor glycemic control and consideration should be given to the patient's ability to manage diabetes at home [34].

Some studies and recommendations are in favor of using the HbA1c value to guide the treatment regimen at discharge - patients with an acceptable glycemic control can be maintained with pre-hospitalization treatment and patients with suboptimal control should intensify therapy [16].

Neurological system

Orthostatic hypotension may be precipitated postoperatively, being it mandatory to do continuous monitoring of blood pressure within 24 hours after any intervention [11].

DISCUSSION

The combination of an increased incidence and an inadequate perioperative approach to diabetes has led to an increased rate of surgical complications, mortality and treatment costs [1].

It is commonly reported that perioperative glycemic control contributes to reducing the morbidity and mortality [22]. In fact, glycemia levels < 180 mg/dl are usually associated with a lower risk of poor surgical outcomes [13]. Several studies have even shown that the risk of complications is related to the severity of hyperglycemia [69, 70].

Abdelmalak et al. [71] demonstrated that preoperative glycemia is associated with mortality in the first year (P <0.001). Frisch et al. [69] also concluded that the risk of death increases in proportion to perioperative glucose levels (P=0.008) and that hyperglycemia is associated with an increase in length of hospital stay (P=0.001), a greater number of cases of infection (P=0.001), acute renal failure and acute myocardial infarction (P=0.005). McConnell et al. [72] also concluded that postoperative hyperglycemia is associated with a higher percentage of surgical site infection. More recently, Kotagal et al. [70] also reported a dose-response relationship between glycemic levels and compound adverse events. Kwon et al. [73] identified a dose-effect relationship between the efficacy of glycemic control with insulin and prognosis, and concluded that perioperative assessment of glycemia and insulin administration are important goals.

Further to this, several studies have also shown the relationship between high values of preoperative HbA1c and surgical outcomes. A recent study by Narayan et al. [74] showed that an HbA1c ≥ 6.5% was associated with a significant increase in the incidence of deep sternal wound infection (P=0.04) and respiratory complications (P=0.01) in patients undergoing coronary bypass. Kallio et al. [75] also had similar conclusions, showing an increase in the rate of complications and a prolongation of hospitalization in patients with uncontrolled HbA1c (P <0.001). In other studies, preoperative values of HbA1c ≥ 6.5% are also associated with a postoperative glycemic variability, an increase in major adverse events [76] and a decrease in intraoperative insulin sensitivity [77].

Thus, glycemic control has been increasingly recognized as a perioperative goal [37], and it is advisable to postpone elective surgeries when the value of glycemia and HbA1c is very high [13]. However, there is no consensus nor sufficient evidence to recommend the postponement from a specific value of HbA1c or fasting glycemia [16, 23].

The literature supports the prevention of hyperglycemia and also hypoglycemia, but the ideal range between these two points remains equally undetermined [13].

In general, it is currently accepted that perioperative normoglycemia (80-120 mg/dl) also increases morbidity and mortality by increasing the rate of hypoglycemia, and that moderate

perioperative glycemic control (140-180 mg/dl) is the one with better results [13].

Bhamidipati et al. [78] showed that moderate glucose (127-179 mg/dl) was associated with lower mortality (P=0.02) and lower incidence of major complications (P <0.001), similar to Duncan et al. [79] who have shown that blood glucose levels between 140 and 170 mg/dl are associated with a decreased risk of adverse events. In a study conducted in an ICU by Finfer et al. [80] it was also shown that intensive glycemic control (81-108 mg/dl) increased cardiovascular mortality (P=0.02) and the number of hypoglycemic seizures (P <0.001), while target values ≤ 180 mg/dl resulted in a decrease in mortality. Another study conducted in an ICU [81] and another meta-analysis [82] also concluded that strict glycemic control was associated with a much higher risk of hypoglycemia with no improvement in mortality.

Thus, AACE and ADA [31] now advise less aggressive therapy for blood glucose targets between 140-180 mg/dl, contrary to previous recommendations. The Society of Critical Care Medicine [83] also places 150 mg/dl as a glycemic target in all non-cardiac patients, and values < 180 mg/dl are accepted by some authors [34, 40].

Likewise, the optimal glycemic management strategy remains undetermined, and there is no consensus regarding how perioperative hyperglycemia should be controlled, being there no sufficient evidence in the literature to guide the use of insulin and a lack of cut-off values [23, 26]. For example, in 2009 the Society of Thoracic Surgeons guidelines [84] recommended the use of insulin infusion for hyperglycemia > 180 mg/dl, whereas in 2012 the Critical Care Society reported that patients with blood glucose > 150 mg/dl should be treated to keep values below this [83].

There is also insufficient evidence on the preoperative management of antidiabetic medication [23]. It is recognized that various recommendations offer a large number of different instructions, and the fear of hypoglycemia often leads to inappropriate practices of stopping all medication [16]. For example, it has been recommended that OADs be discontinued the day before surgery [23, 40], but, on the other hand, for example, the Joint British Diabetes Societies [34] state that metformin may be maintained on the day of surgery if there is no renal injury and the SAMBA [23] states that metformin should be taken the day before but not on the day of surgery.

Given this, there are many areas that require future studies and for which the current information is insufficient and conflicting, being it necessary to develop adequate and well-designed studies to make safer and universal recommendations [23].

Overall, with the use of careful glycemic management strategies, surgical outcomes are similar in diabetics and non-diabetics [37]. Therefore, according to Monteiro et al. [22], the implementation of institutional protocols that promote adequate preoperative assessment, the selection of safe glycemic targets and the minimization of risk factors for postoperative

complications, improve the prognosis of these patients.

In this context, Udovcic et al. [85] revealed that, after the introduction of guidelines, there was an increase in the preoperative (P <0.01) and intraoperative (P <0.01) glycemic monitoring, increased use of insulin during the whole perioperative period (P <0.01) and significantly lower pre and postoperative glycemic mean values (P <0.01). A similar study by Shah et al. [86], also showed that the Hb1Ac value was measured in a higher percentage in a group evaluated after the implementation of guidelines (P <0.01), as well as pre and intraoperative blood glucose monitoring (P <0.001), and an increase in the use of perioperative insulin (P ≤0.04) as well as lower pre and postoperative blood glucose mean levels (P <0.01) were also observed. McCavert et al. [87] also demonstrated that glycemic optimization, based on the use of a hospital protocol, was associated with a 25.4% reduction in perioperative complications, and the authors recommended the use of pre-defined guidelines in all diabetics.

That being said, it is urgent to elaborate proposals of new protocols, to evaluate them and to implement them in all hospital institutions, as well as reevaluating them periodically [29].

Finally, another main problem is that the prevalence of undiagnosed DM is high in hospitalized patients [13]. A study by Abdelmalak et al. [88] showed that, of the 33923 surgical patients analyzed and known as non-diabetic, 10% were undiagnosed diabetics. Sheehy et al. [89] have reached similar conclusions. That is why correct preoperative evaluation is equally essential [8].

KEY LEARNING POINTS

Preoperative

1. The authors recommend a preoperative anesthetic evaluation with medical optimization, risk stratification and an adapted surgical plan.
2. Discontinuation of OADs and fast-acting insulin on the day of surgery is generally advised, and basal and intermediate insulins are usually continued.
3. It is essential to identify all diabetics and prioritize them in the list of surgeries, minimizing the fasting time to about 6 hours.
4. The authors stress the need for frequent glycemic monitoring to ensure that glycemia is in the target range.
5. According to the guidelines, hyperglycemia should be corrected with sliding-scale fast-acting insulin, and hypoglycemia with sugar-rich drinks, glucose tablets or IV glucose, depending on the time remaining for surgery.
6. Cancellation of non-urgent procedures should be considered if patients exhibit metabolic abnormalities, glycemic measurements above 300-500 mg/dl, and/or HbA1c ≥ 8.5-9% or <5%.
7. In the preparation of the diabetic it is also advised to do prayer sign evaluation, cardiovascular evaluation, hemodynamic optimization when there is risk of renal dysfunction, and the promotion of gastric emptying in case of autonomic gastrointestinal disfunction.

Intraoperative

1. The authors recommend the use of IV infusion of regular insulin for glycemic control in major surgeries, and the use of corrective rapid insulin, if necessary, in minor surgery.
2. Fluid replacement should be done with Hartmann's solutions, but in the case of prolonged fasting and/or IV insulin infusion, 5-10% glycosated sera should be given.
3. The guidelines advise blood glucose monitoring every hour and more often when values are outside the target range or suffer variations.
4. According to the most current recommendations, the glycemic target should be between 80-180 mg/dl.
5. In case of hyperglycemia, in minor surgery it is described that this should be corrected with sliding-scale rapid subcutaneous insulin and in major surgeries by increasing the IV infusion rate; if hypoglycemia is suspected, IV infusion of insulin should be suspended and, if necessary, hypertonic glucose IV should be initiated.

6. Loco-regional techniques appear to have advantages over general anesthesia, such as a lower risk of hyperglycemia.
7. In patients at high risk for gastroparesis and aspiration, it is important to consider the use of a rapid-sequence intubation.

Postoperative

1. Early return to oral nutrition is recommended.
2. Multimodal analgesia and antiemetic prophylaxis are also advised.
3. According to the guidelines, the target glycemic range in this period is 140-180 mg/dl.
4. When the patient is able to safely resume food intake, the OADs and insulin can be restored, with the basal-bolus insulin regimen being the most appropriate and there being a need for continuation of IV perfusion in the transition to subcutaneous insulin.
5. In the event of hypoglycemia and if there is no contraindication to oral feeding, the patient should ingest sugar or, if necessary, hypertonic IV glucose should be administered; if oral feeding is not indicated or the patient is unconscious, IV infusion of glucose or administration of glucagon are advised.
6. In case of hyperglycemia, supplemental corrective insulin can be used to restore glycemic values.
7. Before discharge, capillary blood glucose should be checked and the HbA1c value should be used to determine whether pre-hospitalization treatment should be maintained or whether it should be intensified.

CONCLUSION

DM is a growing public health problem and is therefore also very common in surgical patients. However, both diagnosed and undiagnosed DM, negatively affect surgical outcomes.

In this group of patients, the main objective of the perioperative period is to prevent dysglycemia. For this purpose, it has been recommended, in the preoperative period, to do medical optimization and risk stratification; in the intraoperative period, the use of IV insulin infusion and frequent glycemic monitoring with correction of dysglycemia, in order to maintain glycemic targets of 80-180 mg/dl; and in the postoperative period, an early return to oral nutrition and to the initial therapeutic regimen, as well as a pre-discharge therapeutic optimization.

However, this review shows that there are still controversies in this subject and a great shortage of studies that support specific measures and establish universal cut-offs. Therefore, although no single scenario describes what to do with diabetics undergoing surgery, this review leads to the belief that there should be clearer guidelines regarding the perioperative approach and the control of hyperglycemia from pre to postoperative, with attention to the specific needs of these patients, based on better evidence and carried out by multidisciplinary teams. This would not only allow to minimize complications, to promote better glycemic control and to avoid cancellation of surgeries, but also to decrease the percentage of undiagnosed DM.

This review also addresses an issue of growing interest, due to its increasing use - the continuous insulin infusion pumps. In fact, the correct perioperative approach of diabetics using this system is increasingly important, so that they can also achieve the required glycemic control and achieve outcomes comparable to other diabetics. In this way, there should also be more specific guidelines, and continuous promotion of better training of health professionals in this and other issues related to technological development in this area.

With this review, it is also concluded that it is increasingly important that patients with DM have more and better capacity to manage their own disease, so as to facilitate their optimization in the surgical context, which is already, in itself, a constant challenge.

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